Remarks

Applicants note with appreciation the withdrawal of the rejection for lack of enablement and the withdrawal of the rejections for double patenting.

Novelty:

The Rejection of Claims 1, 2, 8, 9, 11, 12, 17,18, 26, 28, 30, 34, 36, 38, 53, 65, 78, 85, 92, 102, and 103 Under 35 U.S.C. §102(b)

The rejection of the stated claims as anticipated by Hanson (US 5,844,107) is maintained because the U.S. Patent and Trademark Office understand that Hanson teaches the same rod-like particles which are the subject of the claims. However, as detailed below, Hanson's rod-like particles have different physical/structural properties.

Hanson teaches relaxed DNA complexes which are rod-shaped. The claimed subject matter is directed to condensed DNA complexes which are rod-shaped. Each of the independent claims recites: "wherein the nucleic acid molecules of the rod-shaped complexes are condensed."

The U.S. Patent and Trademark Office disagrees with Applicants' conclusion that the "only rod-like structures Hanson teaches are fiber-containing complexes which are not condensed as required by the claims....Hanson therefore does not teach the formation of rod-shaped complexes of condensed nucleic acid." The reason that the U.S. Patent and Trademark Office gives for its disagreement is that "Hanson teaches 'electron microscopic results have been indicated as follows:...the structure resulting from condensation are rod-like relaxed toroids of increased size'(col. 62, lines 51-57[1])." Tellingly, the quotation was truncated before the last word in Hanson's sentence. The quotation omitted the parenthetical expression "(Relaxed)." The parenthetical expression is important because Hanson, in the same footnote, characterizes other structures observed by electron microscopy as "(Aggregated)" or "(Condensed)." Thus, Hanson's own characterization of the rod-like relaxed toroids of increased size is "relaxed" and this term is used as an alternative structure to aggregated or condensed. Thus, by Hanson's own characterization, the rod-like relaxed toroids of increased size are

[1] This is in footnote 2 of Table 104.

not condensed. Thus the U.S. Patent and Trademark Office's conclusion that "the examiner believes that the rod-like, relaxed toroids of Hanson satisfy the claim limitations of the instant application" cannot be maintained. The relaxed toroids of Hanson cannot be interpreted to be condensed, contrary to Hanson's own explicit teaching.

The U.S. Patent and Trademark Office points to a teaching in the present application that lists condensation reaction products as including forms of long (100-300 nm) and narrow (10-20 nm) rods and relaxed toroids (~50-100 nm diameter, 10-20 nm width).[2] Merely because two elements, *i.e.,* rods and relaxed toroids, are in a common list, does not make the two elements synonymous. The relaxed toroids of neither Hanson nor the present application are the same as the recited rods of condensed nucleic acid.

Moreover, merely because both Hanson and the subject application teach relaxed toroids does not mean that they both teach rods of condensed nucleic acid. As mentioned above, these are separate and distinct elements in a list in the specification at page 16, lines 1-3.

The U.S. Patent and Trademark Office further uses Hanson's Table 103 as a basis for its conclusion that Hanson teaches the complexes recited in the subject claims in which the nucleic acid molecules of the rod-shaped complexes are condensed. The Office Action quotes an entry from the fourth column of Table 103[3] which discusses rod-like fibers. Office Action at page 6, the full paragraph. The Office Action concludes that this entry does not refer to either "precipitated, aggregated DNA" or to naked DNA fibers[4]. The conclusion is based on Hanson contrasting the rod-like fibers with other descriptions in the specification. However, using similar reasoning, the U.S. Patent and Trademark Office should also conclude that the rod-like fibers do not refer to the rod-shaped complexes of condensed nucleic acid molecules of the subject claims.

The quoted entry from Table 103 is in the fourth column under the heading "Electron Microscopy." In the first column for that same entry, under the heading "State of DNA or DNA/polycation complex," Hanson employs the description: "Relaxed

[2] Specification at page 16, lines 1-3.
[3] "Rod-like fibers (usually 10-20 times the diameter of a naked DNA fiber, i.e., usually 10-20 nm thick, and longer than 60 nm) of DNA and branched toroidal structures of increased size (FIG. 1F)"
[4] "In this quotation, the 'rod-like fibers' are not referring to DNA fibers associated with precipitated, aggregated DNA, because Hanson contrasts the rod-like fibers with naked DNA fibers."

Complex (caused by excess salt)." This term is used distinctly from other entries in the first column, including "Precipitated Complex (caused by polycation if insufficient salt)," "Unimolecular Aggregated Complex," and "Normal DNA (Not complexed)." These are consistent with what the U.S. Patent and Trademark Office concludes from analyzing other parts of the Hanson specification, *i.e.,* the rod-like fibers are not precipitated, aggregated DNA and are not non-complexed DNA. Similarly, using the same reasoning, the Relaxed Complex which is observed by Electron Microscopy to appear as rod-like fibers cannot be "Condensed Complex (caused by polycation)" because this is a separate entry in the first column describing a different "State of DNA or DNA/polycation complex." Thus, contrary to the conclusion reached by the U.S. Patent and Trademark Office at page 6, last line, the PLL-DNA composition having relaxed-toroid forms taught by Hanson is complexed but ***not*** condensed.

Hanson teaches six DNA forms in Table 103. The form with the rod-like fibers is characterized by Hanson as a separate form from the condensed complex. Hanson teaches that the state of the DNA or the DNA-polycation complex of the rod-like fibers is ***not*** condensed.

A careful reading of Hanson indicates that indeed, Hanson does not teach the subject matter recited in the present application. Hanson does not teach a composition comprising complexes that are rod-shaped when visualized by transmission electron microscopy, wherein the rod-shaped complexes have a diameter of 10-20 nm when visualized by transmission electron microscopy, wherein the nucleic acid molecules of the rod-shaped complexes are condensed.

Thus, Hanson does not anticipate the subject matter of claims 1, 2, 8, 9, 11, 12, 17, 18, 26, 28, 30, 34, 36, 38, 53, 65, 78, 85, 92, 102, and 103. Withdrawal of this rejection is respectfully requested.

Obviousness:

The Rejection of Claims 3, 10, 19, 31, 35, 51-53, 63-65, 67,68, 76-78, and 104 Under 35 U.S.C. §103(a) over Hanson, Park, and Schacht

The Rejection of Claims 58-62, 66, 73-75, 79-82, and 122 Under 35 U.S.C. §103(a) over Hanson, Park, and Mao

The Rejection of Claims 4-7, 13-16, 39-42, 54-57, 69-72, 106-109, 114-117 Under 35 U.S.C. §103(a) over Hanson, Park, Schacht, and Kwoh

As detailed above, Hanson does not teach a composition comprising complexes that are rod-shaped when visualized by transmission electron microscopy, wherein the rod-shaped complexes have a diameter of 10-20 nm when visualized by transmission electron microscopy, wherein the nucleic acid molecules of the rod-shaped complexes are condensed, wherein the complexes are colloidally stable in normal saline. None of the secondary references teaches how to obtain such complexes.

Park is cited for teaching the use of PEG on polylysine attached through an amino terminal linkage.

Schacht is cited for teaching a disulfide linkage via a cysteine moiety of polylysine to PEG.

Mao is cited for teaching the lyophilization of complexes and administration to cells.

Kwoh is cited by the U.S. Patent and Trademark Office for teaching that polylysines of all sizes condense plasmid DNA into toroids and rod-shaped structures as shown by electron microscopy ranging in size from 40 to 80 nm for rods. Further, Kwoh is cited by the U.S. Patent and Trademark Office for teaching that PEG conjugation to PLL-DNA makes longer rods and more rods and that size can be measured using electron microscopy. Even so, Kwoh does not teach remaining elements of the claims. Kwoh's complexes are not colloidally stabile in normal saline.

Kwoh teaches the instability of her complexes in a number of different ways. In Table 1, Kwoh compares the size of her polylysine complexes (PLL10K and PLL26K) in water to the size in 0.15 M NaCl. The complexes aggregate in the saline, increasing particle size by 5-fold. See also Fig.3A, where the complexes in NaCl have larger

diameters at all charge ratios. Similarly, Kwoh teaches that PEG-lysine complexes are not colloidally stable in physiological saline. Complexes made with DNA and PLL10K-PEG5K have a diameter of 80.5 nm in water, which increases to 187 nm in saline (see page 185, column 1, lines 12 to column 2, line 3.)

There is no teaching or suggestion that using any particular elements of the secondary reference teachings combined with Hanson's teaching would result in the recited rod-shaped complexes. Nonetheless, the U.S. Patent and Trademark Office urge that the claimed compositions are not "anything more than what has been known in the art." The examiner finds "the compositions of the instant claims to be obvious variants of what has been performed by others skilled in the art."

How are the compositions which are claimed better than Hanson's? As detailed above, Hanson's rod-like particles are relaxed. Such complexes are more susceptible to degradation in nuclease-rich environments, such as serum. In such environments, the complexes of the present invention are more stable. As shown in Figure 18 of the application, poorly condensed DNA is more susceptible to nuclease degradation. How are the compositions which are claimed better than Kwoh's? The compositions of the present invention are stable in normal saline.[5] Again, this is an important characteristic for use in the human body.

Withdrawal of the rejection is respectfully requested because the cited art fails to present a *prima facie* case of obviousness.

Respectfully submitted,

Date: 15 July 2008

By: /Sarah A. Kagan/
Sarah A. Kagan
Registration No. 32,141

Banner & Witcoff, Ltd.
Customer No. 22907

[5]As recited in claims 1, 8, 17, 26, and 28 : "wherein the complexes are colloidally stable in normal saline."